Preparation of Methyl Acetoxypropionate

PREPARATION FROM LACTIC ACID, ACETIC ACID, AND METHANOL

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The conversion of lactic acid into methyl α-acetoxypropionate without the use of acetic anhydride, ketene, or acetyl chloride is described. Acetoxypropionic acid is formed satisfactorily when lactic acid, acetic acid, an entraining agent such as benzene, and an esterification catalyst such as sulfuric acid, are refluxed so that water is removed. Acetoxypropionic acid is transformed into its methyl ester by treatment with either methanol or methyl acetate. The best means for esterifying acetoxypropionic acid consists in passing this acid and methanol vapor countercurrently through a packed tower maintained at 70° to 130° C. The manufacture of methyl α-acetoxypropionate by this method would be particularly advantageous under wartime conditions as it would not require the construction of plants to convert acetic acid into acetic anhydride or ketene.

IN 1935 Burns, Jones, and Ritchie (*3*, *8*) first demonstrated that methyl acrylate, a valuable synthetic rubber (*9*, *10*, *13*, *15*) and resin (*7*) intermediate, can be made in high yields by the pyrolysis (*5*, *12*) of methyl α-acetoxypropionate; it has now become desirable to have efficient and low-cost methods for preparing this diester from lactic acid. An attractive continuous method (*4*), which comprised the conversion of lactic acid into methyl lactate followed by acetylation with acetic anhydride or ketene, was described recently; but this method requires either acetic anhydride or ketene, which are more expensive than acetic acid. The use of acetic acid as the acetylating agent would have the advantages of lowering the cost of methyl acetoxypropionate (assuming comparable yields) and eliminating the need of plant facilities to convert acetic acid into acetic anhydride or ketene. The desirability of using acetic acid as the acetylating agent is increased by the fact that acetic acid as well as methyl acrylate is produced by the pyrolysis of methyl acetoxypropionate:

$$\underset{\text{(I)}}{CH_3COOCH(CH_3)COOCH_3} \xrightarrow{500^\circ\text{ C.}} CH_3COOH + CH_2{:}CHCOOCH_3 \quad (1)$$

At least two approaches to the problem of preparing methyl acetoxypropionate with acetic acid as the acetylating agent can be followed. By the first, methyl lactate is prepared by esterification of lactic acid, and the methyl lactate is acetylated with acetic acid. The second approach comprises the acetylation of lactic acid with acetic acid, followed by esterification of the acetoxypropionic acid (II). Preliminary experiments showed that, although some of the desired diester (I) is obtained, methyl acetate is formed readily when methyl lactate is treated with acetic acid. Since this side reaction cannot occur when lactic acid is acetylated, the possibility of transforming lactic acid into methyl acetoxypropionate by the second route (Equations 2 and 3) was investigated:

$$CH_3COOH + HOCH(CH_3)COOH \longrightarrow \underset{\text{(II)}}{CH_3COOCH(CH_3)COOH} + H_2O \quad (2)$$

$$\underset{\text{(II)}}{CH_3COOCH(CH_3)COOH} + CH_3OH \longrightarrow \underset{\text{(I)}}{CH_3COOCH(CH_3)COOCH_3} + H_2O \quad (3)$$

TABLE I. PREPARATION OF ACETOXYPROPIONIC ACID FROM LACTIC[a] AND ACETIC ACIDS

Expt. No.	Lactic Acid, Moles	Acetic Acid, Moles	Ratio, Acetic: Lactic	Entraining Agent, Ml.	Catalyst, Ml.	Time of Reflux, Hr.	Yield of Acetoxypropionic Acid, %
147	1.0	8.75	8.58[b]	Benzene, 150	H_2SO_4, 1	5.3	55
212	1.0	6.0	6[c]	Benzene, 200	Same	5.5	71.5
215	1.0	16.6	16[c]	Same	Same	10.	74
218	1.0	16.6	16[c]	Same	Same	6.5	78.4
139	6.0	18.0	2.6[b]	Benzene, 300	H_2SO_4, 1.5	25.5	68
314	4.0	8.0	1.7[b]	Benzene, 200	H_2SO_4, 1	15.3	40
316	4.0	12.0	2.4[b]	Same	Same	14.5	55
317	4.0	16.0	3.3[b]	Same	Same	19.5	61
319	4.0	20.0	4.1[b]	Same	Same	18.3	70
321	4.0	24.0	5.0[b]	Same	Same	12.8	67
323	4.0	28.0	6.0[b]	Same	Same	21.0	77
325	4.0	32.0	6.8[b]	Same	Same	14.3	71
173	4.0	20.0	4.0	Same	Same	15.0	61
333	1.0	16.6	15.4[b]	Same	H_2SO_4, 0.25	15.4	60
322	4.0	28.0	7[c]	Isopropyl acetate, 200	H_2SO_4, 1	9.3	67

[a] 80% lactic acid solution was used except in experiment 147, in which 100% acid was used.
[b] Correction made for amount of acetic acid removed with water by entraining agent.
[c] Approximate.

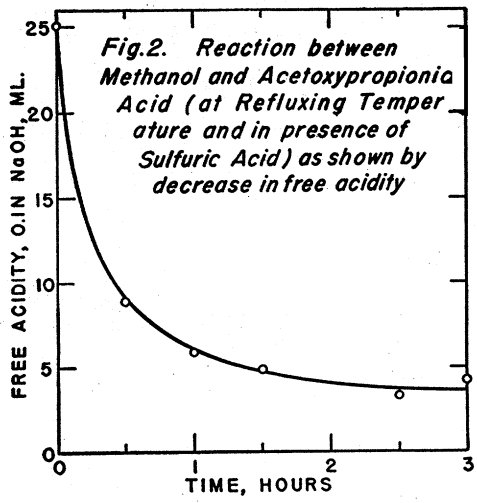

Fig.2. Reaction between Methanol and Acetoxypropionic Acid (at Refluxing Temperature and in presence of Sulfuric Acid) as shown by decrease in free acidity

The acetyl derivative of lactic acid (II) has been prepared by the reaction of lactic acid with acetic anhydride (*2*, *11*) and with acetyl chloride (*1*, *6*), but apparently no previous attempts to acetylate lactic acid with acetic acid have been described.

REACTION OF ACETIC ACID WITH LACTIC ACID

Since lactic acid has a carboxylic acid group as well as an alcohol group, at least two reactions can occur when a mixture of lactic acid and acetic acid is heated and the water of esterification is removed. In the desired reaction, the alcoholic hydroxyl group of lactic acid reacts with the acetic acid to form acetoxypropionic acid. The alcoholic hydroxyl group also reacts with the lactic acid carboxyl group, forming lactyllactic acid (where $x = 2$) and similar linear condensation products (*14*) of lactic acid:

$$HO[CH(CH_3)COO]_x H$$
(III)

Probably the linear condensation products (III) of lactic acid react with acetic acid in two ways. The acetic acid may acetylate the terminal alcoholic hydroxyl group, or it may decrease the chain length of the linear condensation products by acidolysis. Since all the reactions with acetic acid lead to the formation of acetoxypropionic acid, it would be expected that an excess of acetic acid would be helpful. Experience has borne out this expectation.

A commercial, edible grade of 80% lactic acid, which was almost colorless, was used in most of the acetylation experiments. The lactic acid was acetylated by refluxing a mixture of lactic acid, acetic acid, an entraining agent such as benzene, and a small amount of an esterification catalyst such as sulfuric acid, condensing the vapors, and returning the benzene layer to the reaction mixture (in a modified Dean and Stark tube). The reaction was considered complete when approximately one mole of water had been removed for each mole of lactic acid in the reaction mixture. After the mineral acid had been neutralized with anhydrous sodium acetate (usually 4 grams of sodium acetate per ml. of sulfuric acid), the acetoxypropionic acid was distilled under reduced pressure.

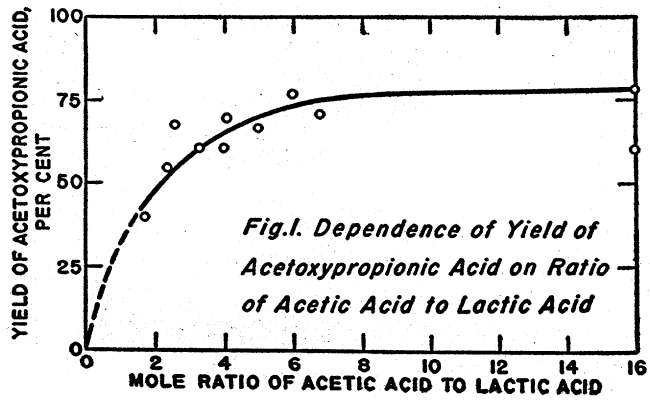

Fig.1. Dependence of Yield of Acetoxypropionic Acid on Ratio of Acetic Acid to Lactic Acid

The results of the acetylation experiments show that acetoxypropionic acid can be made satisfactorily and in high yields by the reaction of acetic acid with lactic acid. The amount of lactic acid converted into acetoxypropionic acid varied with the amount of acetic acid used. The yield of acetoxypropionic acid was approximately 80% when a considerable excess of acetic acid was used (Table I). The dependence of yield upon the ratio of acetic acid to lactic acid is shown in Figure 1. The brown, viscous distillation residues, which probably consist mainly of acetylated condensation products of lactic acid, should be useful as a starting material in making monomeric lactic acid, methyl lactate, or acetoxypropionic acid.

Since both acetic and lactic acids are inexpensive and potentially available in large quantities, acetoxypropionic acid could be made on a large scale at low cost. As ordinarily prepared, this acid is a moderately viscous fluid that supercools easily and is difficult to crystallize unless seeded. When crystallized, the acid is a low-melting solid (*2*). It distills at 75° C. (0.2 mm.), 90° (1 mm.), and 165° to 172° (75 mm.).

REACTION OF ACETIC ACID WITH POLYLACTIC ACID

Acetoxypropionic acid was prepared also by the acidolysis of polylactic acid (III) with acetic acid. The linear condensation polymer of lactic acid was prepared by dehydrating, under 20 mm. pressure, 200 grams of 100% lactic acid containing 2 grams of *p*-toluenesulfonic acid. Water was distilled from this mixture (final temperature of reaction mixture, 150° C.) for several hours; the total distillate, mainly water, was 38.5 grams (approximately 96% dehydration). The distillation residue was then treated with 1000 grams of glacial acetic acid, and the resulting mixture was refluxed for 9.5 hours. After the addition of 3 grams of sodium acetate the mixture was distilled. The yield of acetoxypropionic acid was 26%. The results of this experiment indicate that the esterification of the alcoholic hydroxyl group is more rapid than the acidolysis of the ester group.

REACTION OF ACETOXYPROPIONIC ACID WITH METHYL ACETATE

Because of the high vapor pressure of methyl acetate, the reaction of methyl acetate with acetoxypropionic acid was studied in a closed system. A mixture of acetoxypropionic acid,

TABLE II. METHYL ACETOXYPROPIONATE FROM ACETOXYPROPIONIC ACID AND METHYL ACETATE[a]

Expt. No.	Methyl Acetate, Moles	Temp., °C.	Methyl Acetoxypropionate Conversion, %[b]	Methyl Acetoxypropionate Yield, %[c]
214	1.25	100	33	61
219	2.5	100	33	77
223	2.5	125	40[d]	66[d]
225	2.5	120–130	35	74
226	2.5	140–150	60	84
227	2.5	120–126	54	81

[a] 0.5 mole acetoxypropionic acid and 0.5 ml. concentrated H_2SO_4 used; reaction period, 4 hours.
[b] Acetoxypropionic acid converted into methyl ester.
[c] Per cent of theoretical, based on acetoxypropionic acid destroyed.
[d] Bomb leaked during the experiment.

methyl acetate, and a small amount of sulfuric acid was placed in the glass liner of a metal bomb and heated for 4 hours at different temperatures (Table II). The contents of the bomb were then treated with enough sodium acetate to neutralize the sulfuric acid, and the products were isolated by distillation under reduced pressure.

The highest yield of methyl acetoxypropionate obtained by the reaction of acetoxypropionic acid with methyl acetate was 84% (Table II). Acetic acid also was isolated. The most extreme experimental conditions used (140° to 150° C. for 4 hours) were not drastic. This reaction, which does not require acetic anhydride or ketene, could be employed to prepare methyl acetoxypropionate.

ESTERIFICATION OF ACETOXYPROPIONIC ACID AND METHANOL

Because of the importance of the reaction, the esterification of acetoxypropionic acid and methanol was studied extensively under various conditions. In some of the experiments, mixtures of the two reactants were heated in the liquid phase and then distilled to determine the nature and amounts of the products. In other experiments the esterification was effected by passing methanol vapor and acetoxypropionic acid countercurrently through a packed tower under atmospheric or reduced pressures.

The liquid-phase esterifications were carried out by refluxing a mixture of 0.5 mole of acetoxypropionic acid, 2.5 moles of methanol, and 0.5 ml. of sulfuric acid. At the end of the reaction period the sulfuric acid was neutralized with sodium acetate (2 grams), and the products were isolated by distillation. The course of the reaction was followed by titration of small samples of the reaction mixture to determine the free acidity. The results (Figure 2) show that the free acidity almost reaches its minimum value in 2 hours. High yields of methyl acetoxypropionate were not obtained because of the formation of methyl lactate and methyl acetate. The yields, respectively, of methyl acetoxypropionate, methyl lactate, and methyl acetate were 34, 43, and 36% after 1 hour of refluxing, and 21, 52, and 48% after 3 hours. In both instances the combined yields of the lactic esters were more than 70%. Probably the distillation residues contained polylactic acid (III) or esters of polylactic acid, which should be of some value as a source of monomeric lactic acid, methyl lactate, or acetoxypropionic acid.

Much higher yields were obtained when the esterification was carried out with methanol vapor in a packed tower under nonequilibrium conditions. Slightly different techniques were used at atmospheric and at 100 mm. pressure.

Under a pressure of approximately 100 mm., a mixture of acetoxypropionic acid, methanol, and sulfuric acid was added dropwise into the top of a Pyrex tower (1 × 48 inches) packed with 1/4-inch porcelain Berl saddles and was electrically heated. The temperature of the column was controlled and recorded automatically. Methanol was passed into a heated vaporizing flask, and the vapor issuing from this flask was passed into the bottom of the packed tower. The methanol vapor was passed through the tower as long as acetoxypropionic acid was being passed into the column and until the dry appearance of the packing indicated that all the acetoxypropionic acid had reacted. The vapors withdrawn from the top of the tower, which consisted of methanol, methyl acetoxypropionate, and other volatile products, were passed into the center of a steam-jacketed distillation column packed with small Berl saddles. The methanol and water vapors that passed through this stripping still were condensed. The products of higher boiling points, which were collected at the bottom of the distilling column, were redistilled in a vacuum to determine the amounts of methyl lactate and methyl acetoxypropionate obtained. Yields of methyl acetoxypropionate as high as 72–75% were obtained at temperatures of 80°–100° C. Methyl lactate also was produced (Table III).

When acetoxypropionic acid was esterified with methanol vapor in the packed tower under atmospheric pressure, the procedure was slightly modified. As before, methanol vapor and acetoxypropionic acid were passed countercurrently through the tower, and the vapors withdrawn from the top of the tower were passed into the center of the steam-jacketed distilling column. The methanol distilling from the top of the column was condensed and returned through a liquid seal to the heated vaporizing flask. When the esterification was carried out at temperatures below 108° C., the material collected at the bottom of the distilling column contained water and some methyl lactate and methyl acetoxypropionate, but most of the esters passed downward through the esterification tower and were collected in a flask at the base. The contents of the flasks located at the bottom of both the distillation and esterification columns were distilled under reduced pressure to determine the yields of methyl lactate and methyl acetoxypropionate (Table III).

When esterification was carried out in the packed tower under atmospheric pressure and at temperatures above approximately 108° C., the methanol vapor was recycled and passed through the tower until it appeared that all the acetoxypropionic acid had reacted and passed as ester through the top of the tower into the distilling column. The material collected at the bottom of the column was then distilled to separate the products.

The data in Table III show that moderately high yields of methyl acetoxypropionate were obtained by the methanol vapor method, both under atmospheric and reduced pressures. Most of the combined yields of methyl acetoxypropionate and methyl lactate ranged from 80 to 90%. The combined yields were moderately high even in the absence of an esterification catalyst (experiments 311 and 312).

TABLE III. METHYL LACTATE AND ACETOXYPROPIONATE PRODUCED BY REACTION OF ACETOXYPROPIONIC ACID WITH METHANOL VAPOR IN A PACKED TOWER

Expt. No.	Acetoxypropionic Acid, Mole	H_2SO_4, Ml.	Temp., °C.	Pressure, Mm.	Time, Hr.	Methyl Lactate Conversion, %[a]	Methyl Lactate Yield, %[b]	Methyl Acetoxypropionate Conversion, %[a]	Methyl Acetoxypropionate Yield, %[b]
296	0.5	0.25	97–101	90–110	1.33	..	22	..	58
297	0.5	0.10	95–102	90–110	1.2	..	10	..	72
307	1.0	0.20	82–87	90–110	3.8	..	11	..	75
308	1.0	0.20	93–98	78–95	2.6	..	17	..	72
309	1.0	0.20	98–118	95–130	2.1	..	9	..	72
310	1.0	0.20	115–122	70–110	1.3	..	8	..	65
311	1.0	None	115–122	85–105	6.5	5	8	33	51
295	0.5	0.25	122–135	Atm.	1.8	..	47	..	34
312	1.0	None	128–133	Atm.	3.0	15	24	39	62
313	1.0	0.02	128–136	Atm.	2.0	21	25	46	55
324	1.0	0.05	74–79	Atm.	0.5	3	7	20	50
326	1.0	0.05	82–88	Atm.	0.7	6	10	35	60
327	1.0	0.05	ca. 95	Atm.	0.6	6	11	28	54
328	1.0	0.05	101–108	Atm.	0.7	10	19	31	60
329	1.0	0.05	74–79	Atm.	2.5	7	14	35	71

[a] Per cent of acetoxypropionic acid converted.
[b] Per cent of theoretical, on basis of acetoxypropionic acid destroyed.

DISCUSSION OF RESULTS

The production of methyl acetoxypropionate from lactic acid, acetic acid, and methanol by the methods described here have the advantage of not requiring the use of acetic anhydride or ketene, but the yields are not so high as those obtained by conversion of lactic acid into methyl lactate followed by acetylation with acetic anhydride, as described in the preceding paper. To afford a comparison of the relative merits of the two methods, the materials costs of methyl acetoxypropionate prepared by the two methods were calculated. The prices assumed for the intermediate chemicals may not have been exactly correct, but the same prices were used for both methods and therefore the calculated material costs should be adequate for a preliminary comparison. In making the calculations, the cost of sulfuric acid used as catalyst was not included, and it was assumed that an over-all yield of 85% acetoxypropionic acid could be obtained from lactic acid by treatment of the distillation residues with acetic acid. The other yields assumed in estimating relative costs were: 75% methyl acetoxypropionate and 10% methyl lactate in the esterification of acetoxypropionic acid, 90% methyl lactate in the esterification of lactic acid, and 96% methyl acetoxypropionate in the acetylation of methyl lactate. All yields were calculated on the basis of unrecovered starting materials.

The calculated cost of materials indicated that the acetoxypropionic acid method of making methyl acetoxypropionate is somewhat more expensive (approximately 2 cents per pound) than the previously described methyl lactate method (*4*). The acetoxypropionic acid method, however, has the advantage of not requiring plants for the manufacture of acetic anhydride or ketene. Owing to the shortage of alloys and other construction materials, this advantage would be highly important under wartime conditions if large quantities of methyl acrylate were manufactured by the pyrolysis of methyl acetoxypropionate.

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